New Macrolides or New Quinolones as Monotherapy for Patients With Community-Acquired Pneumonia

Our Cup Runneth Over?

For the past decade, the atypical pathogens as a group (Legionella pneumophila, Chlamydia pneumoniae, and Mycoplasma pneumoniae) have become accepted as relatively common causes of pneumonias in both the outpatient and inpatient setting. As a result, recommendations for more widespread use of antimicrobial active against these pathogens have become well-accepted.1,2

In the community-acquired pneumonia study by Mundy and colleagues in this issue of CHEST (see page I201), only 7.5% of the patients were classified as being infected by an atypical pathogen. Almost 40% of these patients failed to receive antimicrobial therapy considered to be active against Legionella (tetracyclines, macrolides, quinolones) and yet none died. The authors concluded that routine administration of macrolides may not be necessary.

However, some caution must be exercised regarding the authors’ conclusion of the necessity for coverage against the atypical pathogens. The atypical pathogen that is most virulent is Legionella, which was present in only 3.4% of their study population. It has been well-established that mortality rates for both M. pneumoniae and C. pneumoniae are low, even when antibiotic therapy is not given. In fact, the primary effect of administration of antibiotics against M. pneumoniae is not to lower mortality but to decrease the duration of cough and other symptoms.

We believe that the incidence of Legionella infection is cyclic as has been shown for M. pneumoniae. The frequency of Legionella pneumonias seen in our community has ranged from 1 to 9% in different years. Had the incidence of legionellosis in the study by Mundy and colleagues been higher, we wonder if the mortality rate might also have been higher. Circumstantial data from uncontrolled studies suggest that delay of appropriate antibiotic therapy can be linked to increasing mortality.3-5

Major developments in antimicrobial therapy have occurred in the 5 years since the study by Mundy and coworkers was conducted. Thus, the issue that Mundy and colleagues raised as to whether addition of a macrolide (erythromycin) is cost-effective and that perhaps B-lactam therapy as monotherapy is sufficient given the low mortality observed in their study, has become less relevant to the physician or hospital pharmacist. Both newer macrolides and newer quinolones that are parenteral are now commercially available to physicians (Table I), and in many ways, superior to erythromycin, the only antibiotic active against the atypical pathogens that was used by the authors in their study conducted from 1990 to 1991.

First, the newer macrolides and newer quinolones not only have superior in vitro activity against the three atypical pathogens,6-7 but most also have superior in vitro activity when compared to erythromycin for Haemophilus influenzae and Moraxella catarrhalis. Second, the newer macrolides and quinolones can be given once or twice daily. Azithromycin need only be given for 5 to 10 days rather than the 7 to 21 day range of erythromycin. Thus, compliance, a factor of underestimated importance, is easier with these new agents. Third, controlled randomized clinical trials have validated the efficacy of the newer macrolides and quinolones; they are comparable to the standard B-lactam agents for empiric therapy for community-acquired pneumonia, in both outpatient and hospitalized patients.8-12 Fourth, both the newer macrolides and quinolones have fewer gastrointestinal side effects than erythromycin.13 Fifth, surprisingly, the cost of the 4-g daily dose for a course of parenteral erythromycin often recommended for Legionnaires’ disease is moderately expensive and comparable or even more expensive than the cost required for the newer macrolides.14

Thus, the issue is no longer whether the addition of erythromycin to a B-lactam regimen is required as suggested by Mundy and colleagues, but whether monotherapy with a macrolide or a quinolone can replace the combination of B-lactam agent plus erythromycin! The potential Achilles’ heel of both new macrolide and quinolone regimens deals with antibiotic resistance, a theoretical concern that has become a clinical reality. The penicillin-resistant pneumococci are often resistant in vitro to both erythromycin and the newer macrolides. The major advantage of the new quinolones is that they are active in vitro against the penicillin-resistant pneumococci in contrast to the cephalosporins, B-lactam/β-lactamase inhibitor agents, and the macrolides. Clinical experience will be needed to demonstrate if the in vitro superiority of the newer quinolones against penicillin-resistant pneumococci translates

References

Table 1--New Macrolides and New Quinolones

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<tr>
<th>Macrolides</th>
<th>Quinolones</th>
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<tbody>
<tr>
<td>Azithromycin*</td>
<td>Grepafloxacin</td>
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<tr>
<td>Clarithromycin</td>
<td>Levofloxacın*</td>
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<tr>
<td>Daptomycin</td>
<td>Sparfloxacin</td>
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<tr>
<td>Roaxithromycin</td>
<td>Trovafoxacin*</td>
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*Parental form available in United States.

into clinical superiority. In our limited experience, azithromycin proved to be effective clinically even if patients were infected with pneumococci that were moderately resistant in vitro to azithromycin.9

The disadvantage of the new quinolones is that their broad spectrum of activity against aerobic Gram-negative bacilli is not necessarily an advantage since such organisms are rare in immunocompetent patients with community-acquired pneumonia.13-15 However, widespread use may accelerate the emergence of quinolone-resistant Gram-negative bacilli rendering ciprofloxacin and other quinolones less useful. Thus, these newer quinolones may be more appropriate for community-acquired pneumonia in patients admitted to ICUs, nursing home pneumonias, and nosocomial pneumonias in which coverage against aerobic Gram-negative bacilli is a clear-cut advantage.

The prices for these newer agents as they are released into the market will be a factor in whether their usage becomes widespread. Finally, the potential for emergence for resistance needs to be carefully considered and continually monitored. In the meantime, the physician does not lack for resources against pathogens of community-acquired pneumonia.

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References

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13 Vergis EN, Yu VL. Macrolides are ideal for empiric therapy of community-acquired pneumonia in the immunocompetent host. Semin Respir Infect 1997; 12:327-28

Cystic Fibrosis

When To Consider Lung Transplantation?

Lung transplantation has become an accepted therapeutic option for patients with cystic fibrosis (CF) and end-stage lung disease. This is apparent by the rising number of lung transplants performed each year, as well as the growing number of patients listed for transplantation. Unfortunately, the number of lung donors has not realized similar growth; as the waiting list has grown at a seemingly exponential...